

Amendments to the Specification

On page 13, please substitute for the paragraph beginning on line 5 and ending on line 29, the following paragraph:

-- "Conservatively modified variations" of a particular nucleic acid sequence refers to those nucleic acids which encode identical or essentially identical amino acid sequences, or where the nucleic acid does not encode an amino acid sequence, to essentially identical sequences. Because of the degeneracy of the genetic code, a large number of functionally identical nucleic acids encode any given peptide. Such nucleic acid variations are ~~Asilent~~ silent, @ which are one species of ~~Aconservatively~~ conservatively modified variations. @ One of skill will recognize that each codon in a nucleic acid (except AUG, which is ordinarily the only codon for methionine) can be modified to yield a functionally identical molecule by standard techniques. Accordingly, each ~~Asilent~~ silent variation @ of a nucleic acid which encodes a peptide is implicit in any described amino acid sequence. Furthermore, one of skill will recognize that individual substitutions, deletions or additions which alter, add or delete a single amino acid or a small percentage of amino acids (typically less than 5%, more typically less than 1%) in an encoded sequence are ~~Aconservatively~~ conservatively modified variations @ where the alterations result in the substitution of an amino acid with a chemically similar amino acid. Conservative substitution tables providing functionally similar amino acids are well known in the art. The following six groups each contain amino acids that are conservative substitutions for one another:

- 1) Alanine (A), Serine (S), Threonine (T);
- 2) Aspartic acid (D), Glutamic acid (E);
- 3) Asparagine (N), Glutamine (Q);
- 4) Arginine (R), Lysine (K);
- 5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V); and
- 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W).

ATTORNEY DOCKET NO. 14114.0327U2
APPLICATION NO. 09/171,432

See also Creighton (1984) *Proteins* W.H. Freeman and Company. --